Specialty Conference

From Cyanotic Infant to Acyanotic Adult—The Odyssey of Blue Babies

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In the past two decades we have witnessed the maturing of diagnostic and surgical skills in the management of congenital heart disease. Although longevity and quality of life have improved, cures are few; varying degrees of postoperative medical supervision are therefore needed. This new patient population of adults requiring long-term medical care continues to increase. Proper management of such patients can be taxing, requiring knowledge not only of the preoperative disease but also of the nature and effects of surgical intervention and of the presence, type and extent of late postoperative residua and sequelae. The tetralogy of Fallot is taken as a model because it is well known in both pediatric and adult medicine, because intracardiac repair includes a wide range of techniques and because postoperative residua and sequelae comprise a broad spectrum of patient care concerns.

JOSEPH K. PERLOFF, MD:* *In 1939 Dr John Hubbard, a Boston pediatrician, diagnosed patent ductus arteriosus in a child and Dr Robert Gross, a pediatric surgeon, ligated the duct. Dr Helen Taussig conceived the idea of creating a "patent ductus" in cyanotic children suffering from deficient pulmonary blood flow. Five years later in Baltimore, she made the diagnosis of tetralogy of Fallot, and Dr Alfred Blalock, an experienced vascular surgeon, turned down a subclavian artery and sutured its end to the side of the pulmonary artery, establishing the Blalock-Taussig anastomosis. (Dr William P. Longmire, Emeritus Professor and Chairman, Department of Surgery, UCLA School of Medicine, was Dr Blalock's first assistant at this historic operation.) Thus began a therapeutic era that brought together cardiologists and cardiac surgeons in what proved to be one of the most successful rehabilitation programs that medicine has witnessed.*[1] *Two new disciplines were created, pediatric cardiology and cardiovascular surgery, which have long since come of age. Although we can reflect on the past with considerable satisfaction, we are now obliged to look ahead and redefine our goals.*

Immense technical resources of contemporary medi-

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cine are at our disposal, permitting remarkably precise anatomic and physiologic cardiac diagnoses and astonishing surgical feats. Survival patterns have been affected, often profoundly. What do we seek to accomplish with these formidable capabilities? The answer is clear: not merely long-term survival, but improved quality of life. Cardiac surgical intervention remains the most dramatic and useful therapy for patients with congenital heart disease. Complete cures are few, however, and postoperative medical supervision almost always remains important if not obligatory. Proper care of adults with postoperative congenital heart disease requires knowledge not only of the nature and effects of the surgical intervention, but also of the presence, type and extent of postoperative residua and sequelae. The ideal total correction (complete cure) is rarely achieved, and it is confined to two conditions: division of an uncomplicated, nonpulmonary-hypertensive patent ductus arteriosus and perhaps, but not necessarily, closure of an uncomplicated ostium secundum atrial septal defect in childhood. All other surgical repairs provide palliation, albeit sophisticated palliation. These operations leave behind certain obligatory abnormalities, some trivial, others serious, while they prolong life and improve its quality.

This conference focuses on the tetralogy of Fallot as a means of illustrating and discussing preoperative problems, surgical management and late postoperative benefits, residua and sequelae. The selection was made for several reasons. First, natural survival ranges from infancy to or beyond middle age, making the tetralogy the most frequent cyanotic malformation seen in adults. Second, surgical intervention in Fallot's tetralogy is the earliest "blue baby" operation, and the original operation is still commonly done. Third, the complexity of intracardiac repair requires a wide range of techniques as the anomaly varies from acyanotic to pulmonary atresia. Fourth, the postoperative benefits are gratifying, but residua and sequelae of operation encompass a broad variety of concerns.

Dr William F. Friedman will discuss the preoperative problem from its inception at birth or in early infancy. Dr Hillel Laks will report on palliative (shunt) operations and intracardiac repair. Dr John S. Child will focus on the benefits of a surgical procedure, the complications of shunts and the residua and sequelae of intracardiac repair.

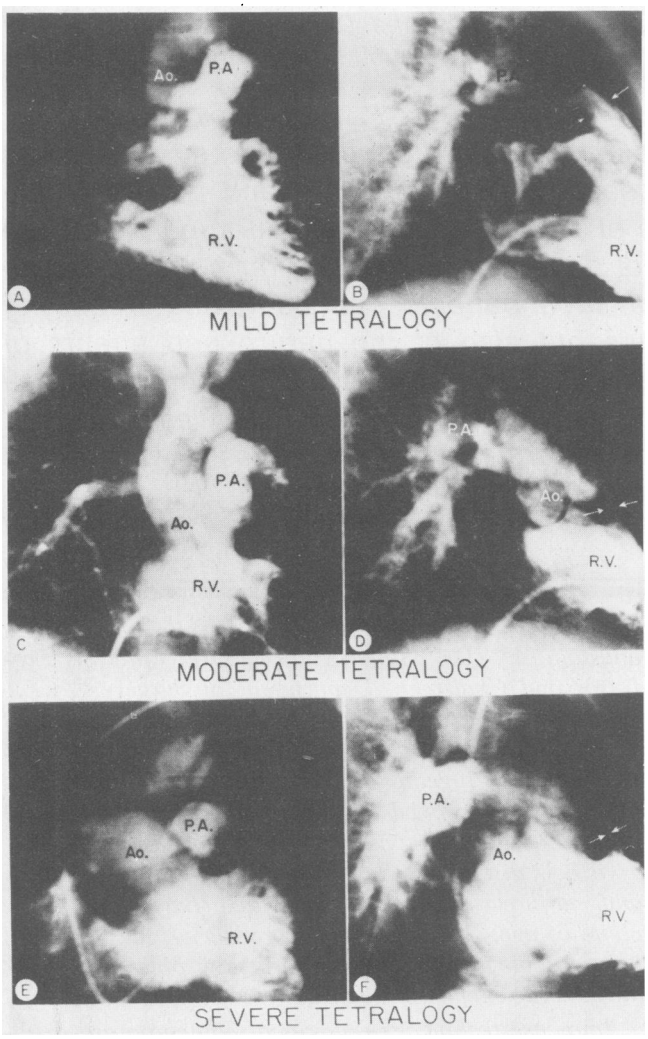

Figure 1.—Frontal **(left panels)** and lateral **(right panels)** views of right ventriculograms in children with tetralogy of Fallot, showing simultaneous opacification of the pulmonary artery (PA) and aorta (Ao). In the lateral frames, the arrows indicate the site and severity of infundibular obstruction. RV = right ventricle

The Preoperative Problem From Its Inception in Infancy

WILLIAM F. FRIEDMAN, MD:* The four anatomic components of the tetralogy of Fallot are ventricular septal defect, obstruction to right ventricular outflow, aortic override (straddle) of the ventricular septal defect and right ventricular hypertrophy. The basic anomaly is believed to result from an anterior deviation of the infundibular ventricular septum away from its usual location in the heart between the limbs of the trabecular septum. The ventricular defect is typically large and located just below the right cusp of the aortic valve separated from the pulmonic valve by the crista supraventricularis.[2,3] The aortic root may be displaced anteriorly, overriding the septal defect but, as in a normal heart, lying to the right of the pulmonary artery. In most cases, the overriding of the aorta is due to the subaortic location of the ventricular septal defect.

The severity of obstruction to right ventricular outflow is the principal determinant of the clinical presentation. The degree of hypoplasia of the outflow tract of the right ventricle varies from mild to complete (pulmonary atresia) (Figures 1 and 2). The infundibulum always becomes narrower. Pulmonary valve stenosis and supravalvar and peripheral pulmonary arterial obstruction may coexist, and unilateral absence of a pulmonary artery (usually the left) occurs in a few patients. Circulation to the abnormal lung is by systemic arterial collaterals.[4-7] Atresia of the pulmonic

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valve, infundibulum or main pulmonary artery is occasionally referred to as "pseudotruncus arteriosus." True truncus arteriosus with absent pulmonary arteries (type 4) differs from Fallot's tetralogy in which pulmonary artery branches are present but are perfused by systemic arterial collaterals or a patent ductus arteriosus (Figures 3 and 4[8]). A right-sided aortic arch and descending aorta occur in about 25% of patients who have tetralogy of Fallot. The coronary arteries may have variations that are surgically important.[9] The anterior descending artery sometimes originates from the right coronary artery, which may also give rise to a left branch coursing anterior to the infundibulum; a single left coronary artery may give rise to a branch that crosses the outflow tract of the right ventricle. Associated cardiac anomalies occur in about 40% of patients[10]; associated noncardiac anomalies are present in 20% to 30% of patients.[11]

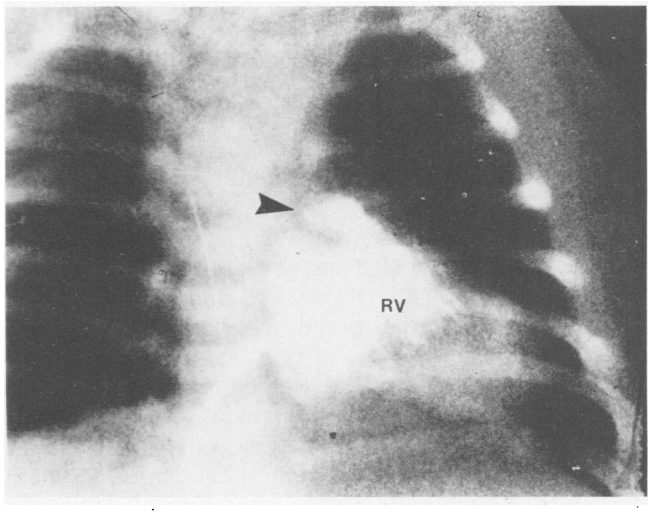

Figure 2.—A frontal view of a right ventriculogram in a 2-day-old infant with tetralogy of Fallot and pulmonary atresia. The right ventricular outflow tract **(arrow)** ends blindly. RV = right ventricle

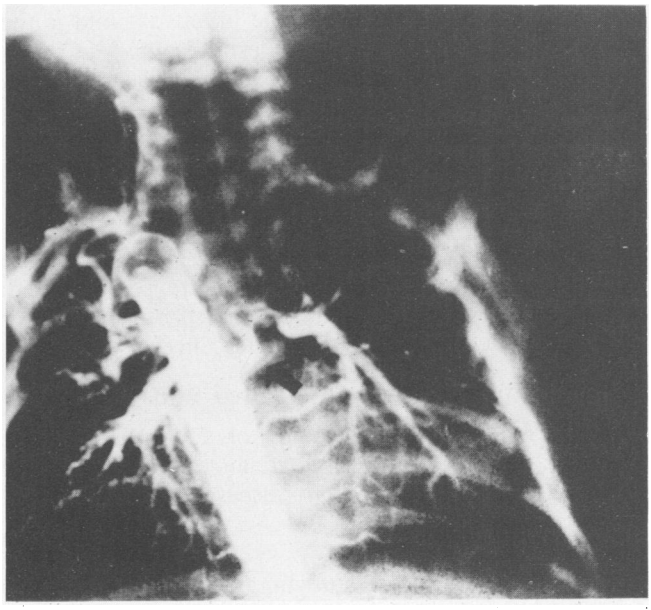

Figure 3.—A descending thoracic aortogram shows abundant systemic collateral arteries providing pulmonary blood flow in a patient with tetralogy of Fallot and pulmonary atresia.

Hemodynamic Disturbances

The relation between resistances to blood flow from the ventricles into the aorta and into the pulmonary artery plays a major role in determining the hemodynamic and clinical picture.[8] Thus, the severity of obstruction to right ventricular outflow is of fundamental importance. When right ventricular outflow tract obstruction is severe, pulmonary blood flow is greatly reduced and a large volume of unsaturated systemic venous blood is shunted from right to left across the ventricular septal defect into the aorta. Severe cyanosis and polycythemia occur and the sequelae of systemic hypoxemia are prominent. At the opposite end of the spectrum, the term "acyanotic" tetralogy of Fallot is often used to describe an interventricular communication with relatively mild obstruction to right ventricular outflow and little or no venoarterial shunting. In many infants and children, the obstruction is initially mild but progressive, so that early in life pulmonary blood flow exceeds systemic flow and the clinical picture resembles simple ventricular septal defect.

Few children with tetralogy of Fallot remain asymptomatic or acyanotic; most are cyanotic from birth or cyanosis develops before 1 year of age. The earlier the onset of hypoxemia, the more severe the outflow tract stenosis. Dyspnea on exertion, clubbing and polycythemia are the rule. After exertion, children with tetralogy characteristically squat. An analogous posture may be beneficial in infancy; many of these cyanotic babies prefer to lie in a knee-chest position.

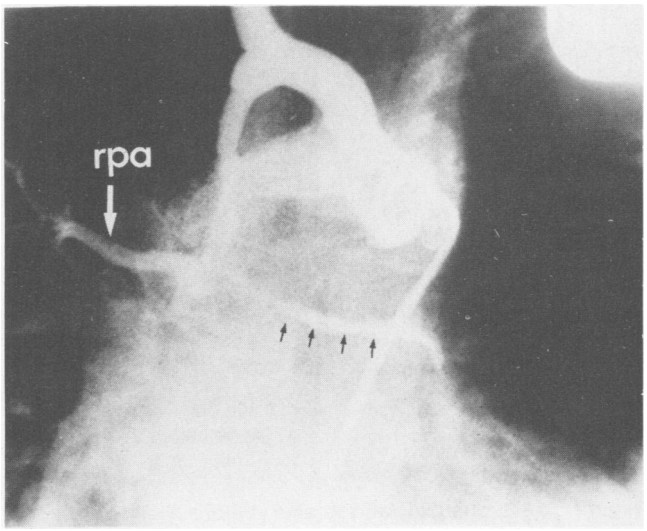

Figure 4.—Selective contrast injection into a systemic collateral artery visualizes the "gull-wing" configuration of hypoplastic right (rpa) and left pulmonary arteries **(arrows)** in a patient with tetralogy of Fallot and pulmonary atresia. (From Friedman[8]; reproduced by permission from WB Saunders Company.)

Episodic spells of intense, transient increases in cyanosis related to a sudden increase in venoarterial shunting and reduction in pulmonary blood flow usually have their onset between 2 and 9 months of age and constitute an important threat to survival. Attacks are not restricted to patients with severe cyanosis and are characterized by anxiety, hyperpnea and deepening cyanosis, progress to limpness and syncope and occasionally terminate in convulsions, cerebrovascular accidents and death. These spells result from an abrupt reduction in pulmonary blood flow.[8] This reduction is precipitated by an abrupt fall in systemic vascular resistance or an acute increase in right ventricular outflow obstruction (augmented contraction of the hypertrophied outflow tract muscle) or a decrease in right ventricular cavity volume due to tachycardia. The carbon dioxide partial pressure (P_{CO_2}) rises, while oxygen partial pressure (P_{O_2}) and pH fall. Treatment consists of administering oxygen, placing the child in the knee-chest position and administering morphine sulfate. Additional medications include intravenously given sodium bicarbonate to correct the acidemia, α-adrenergic-receptor stimulants such as phenylephrine hydrochloride or methoxamine hydrochloride to raise peripheral resistance and diminish right-to-left shunting and β-adrenergic-blocking agents that reduce cardiac sympathetic tone, depress cardiac contractility and increase right ventricular volume by reducing heart rate.

Preoperative Evaluation

Cardiac catheterization and selective angiocardiography are needed not only to confirm the diagnosis and assess the magnitude of right-to-left shunting but, most importantly, to establish the architecture of the right ventricular outflow tract, the pulmonary arterial branches and the anatomy of the coronary arteries.[3,12] Axial cineangiography, particularly using the sitting-up projection, facilitates evaluation of the pulmonary outflow tract and main branches. The preoperative assessment of tetralogy of Fallot with pulmonary atresia must include delineation of the arterial supply to both lungs by selective visualization of systemic collateral arteries. Pulmonary arteries may opacify only after the systemic collateral arteries are cleared of contrast material. Patients with pulmonary atresia should not be ruled out for intracardiac correction unless main pulmonary arteries are clearly inadequate.[4-7] Occasionally, injection of a contrast agent through a catheter in the pulmonary venous capillary wedge position is needed to visualize the pulmonary arteries.[6]

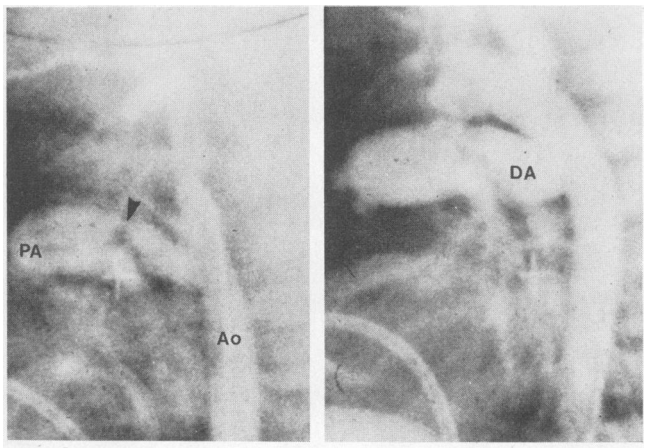

Figure 5.—Sequential aortograms before **(left panel)** and after **(right panel)** intravenous infusion of prostaglandin E_1 in a newborn with ductus arteriosis (DA)-dependent pulmonary blood flow and tetralogy of Fallot. The ductus is constricted in the left panel **(arrow)**, but dilated by the prostaglandin E_1 in the right panel. The dilatation of the ductus arteriosus provided more adequate pulmonary blood flow and improved oxygenation. PA = pulmonary artery, Ao = aorta

Management

Among the factors that complicate the management of patients with Fallot's tetralogy are erythrocytosis, iron deficiency anemia, coagulation disorders, infective endocarditis, paradoxic embolism, cerebral infarction or abscess and paroxysmal hypercyanotic spells discussed earlier. In infants with pulmonary atresia, cardiac catheterization is often done as an emergency. Because survival in this setting usually depends on patency of the ductus arteriosus, intravenous infusion of prostaglandin E_1 (0.1 mg per kg of body weight per minute) may dramatically reverse clinical deterioration and improve arterial blood gases and pH (Figure 5).[12-14]

Primary correction is advisable at some point in the natural history for almost all patients who have tetralogy of Fallot.[15] Early intracardiac repair, even in infancy, is currently advocated in most centers properly equipped for infant cardiac operations.[14] Successful early correction avoids progressive infundibular obstruction, acquired pulmonary atresia, delayed growth and development and complications due to hypoxemia and polycythemia. The size of the pulmonary arteries rather than the age or size of the infant or child is the most important determinant in establishing candidacy for primary repair. Pronounced hypoplasia of the pulmonary arteries is a relative contraindication for an early corrective surgical procedure. When this problem is present, a palliative operation designed to increase pulmonary blood flow is recommended and usually consists of a systemic arterial-pulmonary arterial shunt. Transventricular infundibulectomy or valvotomy are additional palliative procedures but are seldom used. Primary correction can then be carried out at a lower risk later in childhood or in adolescence.

Surgical Interventions—Palliative and Corrective

HILLEL LAKS, MD:* Tetralogy of Fallot exemplifies many of the challenges and advances in the surgical treatment of congenital heart disease.

History

In 1777 Sandifort,[16] studying an autopsied patient who had what came to be known as the tetralogy

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of Fallot, pointed out that the patent ductus arteriosus may have reduced cyanosis. A correlation of the degree of cyanosis with the amount of pulmonary blood flow was recognized by Helen Taussig,[17] who collaborated with Alfred Blalock to develop the subclavian-to-pulmonary artery shunt. This operation, first done successfully on November 29, 1944, was followed by the development of the Potts shunt,[18] the Glenn shunt[19] and the Waterston shunt.[20] In 1948 Brock[21] successfully applied a procedure, first proposed by Doyen in 1913,[22] in which a punch-type instrument was used to do an infundibulectomy.

Total correction of tetralogy of Fallot was first accomplished in 1954 by Scott and associates[23] using hypothermia and circulatory arrest. In 1955 Lillehei and co-workers[24] successfully corrected intracardiac defects using cross circulation. This pioneering work was advanced by Kirklin and colleagues,[25] Kay and associates[26] and others who established the current techniques of repair with cardiopulmonary bypass. With the advances in surgical technique and postoperative care, the mortality in tetralogy of Fallot has been greatly reduced in the past 25 years; intracardiac operation is now done in early infancy.

Palliative Versus Corrective Operation

The surgical treatment of tetralogy of Fallot has evolved from the period during which only palliative measures were available for increasing pulmonary blood flow to the current use of corrective surgical repair. As the results improved, correction was applied to younger infants, leading to considerable debate about the optimal timing for surgical treatment. Some prefer creation of a palliative shunt in infancy followed by correction at a later age.[27] Others recommend total correction in a symptomatic infant regardless of age.[28,29] Proponents of early correction point out that the mortality of the shunt procedure must be added to the mortality of subsequent repair.[28,30] In addition, the shunt may result in stenosis of the pulmonary artery and increased pulmonary vascular resistance; takedown of the shunt may complicate the corrective procedure. Early correction may avoid the deleterious effects of outflow tract obstruction on right ventricular function.[28,31]

Against early correction is the increased risk of operation in which there is a reported mortality of 25% to 67% in the first three months of life.[28,32] In contrast, palliative procedures can be done with a relatively low risk in patients under the age of 6 months.[33,34] Corrective operations undertaken in a child 1 or 2 years of age or older, with or without a palliative shunt, have a low risk of mortality.[27,32,33]

Our practice is similar to that proposed by Kirklin and associates[32] and takes into account the age of a patient and the anatomy of the lesion. In patients younger than 3 months of age a shunt is usually preferred. However, if the obstruction is predominantly due to a spastic infundibulum in a patient presenting with cyanotic spells, propranolol may be given until the age of 3 to 6 months at which time correction can be done. In patients between the ages of 3 and 6 months, the decision as to which procedure to use is based on the anatomy. If the obstruction is mainly infundibular, with a good-sized annulus and pulmonary arteries, correction is the procedure of choice. If the annulus and pulmonary arteries are small, a shunt operation is done because a transannular patch is not well tolerated in small infants. In patients older than 6 months, correction is done, if necessary, with a transannular patch.

Palliative Operation

The commonest form of palliation for tetralogy of Fallot is a systemic-to-pulmonary artery shunt.[35] Infundibular resection using a closed technique is no longer done. The Potts shunt has been largely abandoned because of a tendency to excessive pulmonary blood flow and the difficulty in takedown of the shunt during a corrective procedure.[36] The Waterston shunt is still used by some, particularly in small infants. It is also associated with excessive pulmonary blood flow, however, and frequently results in pulmonary artery constriction requiring reconstruction of the artery during a corrective surgical procedure.[37] The shunt of choice, even in a neonate, remains the Blalock-Taussig shunt.[33] Excellent results have also been obtained with polytetrafluoroethylene grafts placed between the subclavian artery and the pulmonary artery.[38]

In small infants with a pulmonary artery-to-aorta ratio of less than 0.3, Tucker and associates[15] inserted a pericardial outflow-tract patch without closing the ventricular septal defect; among nine infants one death occurred. Further experience is needed to prove that this procedure can be done with results comparable with the palliative shunt.

Results of Palliative Shunts

The younger a patient, the greater the risk with a palliative shunt. One series with excellent results reports an operative mortality of 6% in infants 1 month of age, 4% in those at 3 months, 3% at 6 months and 2.5% at 12 months.[34] The longevity of palliation after a shunt procedure varies according to the age at which the operation is done and the type of shunt. For the Blalock-Taussig and polytetrafluoroethylene graft shunts created in the first months of life, the duration of palliation seems to be about 18 months. In an older child, many years of palliation can be achieved with a Blalock-Taussig shunt.[39]

Corrective Operation

The corrective procedure is done using a median sternotomy incision. In female patients a submammary skin incision with a median sternotomy may be used.[40] In infants weighing less than 6 kg, the procedure is done during deep hypothermia and circulatory arrest. The aorta is cannulated directly, and if circulatory arrest is to be used, a single cannula is placed in the right atrium. If continuous bypass is used, the superior and

inferior venae cavae are cannulated separately through the right atrium and snared. A prior Blalock-Taussig shunt is ligated immediately before instituting bypass. If a Potts shunt is present, it is occluded by finger pressure while cardiopulmonary bypass is instituted and the blood rapidly cooled. The left pulmonary artery is then opened longitudinally, and, if necessary, under circulatory arrest the shunt is closed and the pulmonary artery reconstructed.[41] The Waterston shunt is taken down after commencing bypass and cross clamping the aorta.[42] The pulmonary artery may need reconstruction with a pericardial patch.

Cardiopulmonary bypass is instituted using moderate hemodilution (hematocrit 25%), with blood cooled to 20°C or 28°C, depending on the age of the child. In smaller infants, lower temperatures are used and the repair done either under circulatory arrest or under low flows to achieve optimal visualization of the operating field. The atrial septum is inspected and a patent foramen ovale or atrial septal defect closed either through the tricuspid valve or through a separate right atrial incision.

The incision in the right ventricle (Figure 6)[43] depends on the anatomy delineated by angiography. If it is clear that a transannular path will be needed, a vertical incision is made in the right ventricular outflow tract and, after inspection and measurement of the annulus, the incision is extended to the bifurcation of the pulmonary artery. If the pulmonary arteries and annulus are adequate and the obstruction is mainly infundibular, an oblique or transverse incision is made in the right ventricular outflow tract, avoiding large coronary artery branches. If it is not clear whether a transannular patch will be needed, a vertical or slightly oblique incision is made, permitting extension across the annulus if necessary.

In the presence of an anomalous left anterior descending coronary artery arising from the right coronary artery (in about 5% of patients with tetralogy of Fallot), special considerations apply (Figure 6). If the annulus does not need to be enlarged, a transverse incision can be made below the coronary artery, or a vertical incision can be made and the artery mobilized to permit insertion of the tip of the subannular patch below the anomalous vessel. If the annulus is restrictive, a valved conduit is used to bypass the obstruction.

The technique for intracardiac repair is described and shown in Figure 7. After resection of the outflow tract obstruction, including the septal and parietal bands and a portion of the crista supraventricularis, attention is turned to the pulmonary valve. If there is fusion of the commissures, this can be incised carefully from below. The annulus is measured with Hegar dilators and its diameter is compared with the normal valve sizes prepared by Pacifico and associates.[44] If the diameter is less than the 50% confidence limits for the patient's age, a transannular patch will be needed; in this case the incision is extended across the annulus to the bifurcation of the pulmonary artery. The ven-

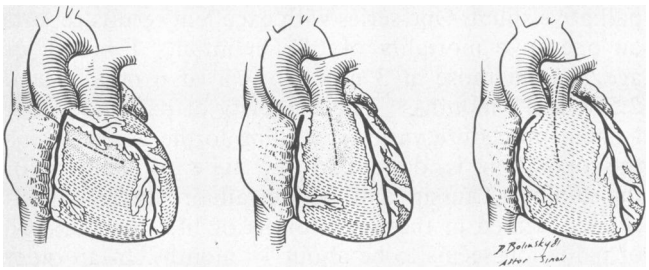

Figure 6.—Three right ventricular incisions used in the repair of tetralogy of Fallot. **Left,** An oblique or transverse incision is used if angiograms show that a transannular patch will not be needed because the obstruction is mainly infundibular and the pulmonary valve and annulus are not narrowed. This incision is also chosen in the presence of an anomalous left anterior descending coronary artery arising from the right coronary and when the pulmonary annulus does not need enlargement. **Middle,** A vertical incision extending up to, but not across, the annulus is used when it is uncertain whether a transannular patch will be needed. **Right,** When the annulus needs enlargement, the incision is extended up to the bifurcation of the pulmonary artery and a transannular patch inserted. (From Laks[43]; reproduced by permission from Appleton-Century-Crofts.)

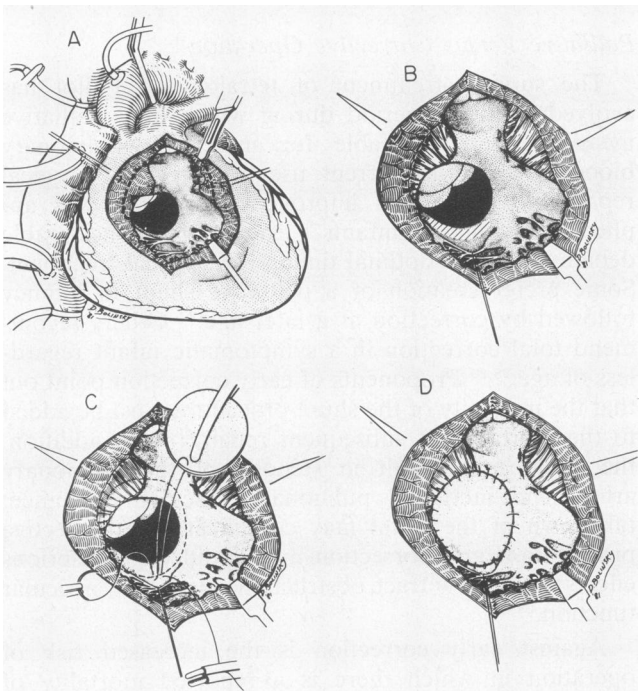

Figure 7.—Technique of repair for tetralogy of Fallot. **A,** The ventricular septal defect is exposed through a vertical right ventriculotomy. The dotted line indicates the resection of the parietal and septal bands. Restricting muscle bands are divided. **B,** Exposure of the ventricular septal defect. The aortic valve is clearly seen. The area of the conduction tissue, which should be avoided, is indicated by the cross-hatching. **C,** A running suture line of Prolene (Ethicon Inc, Somerville, NJ 08876) is used to close the defect. The suture line is below the area of the conduction tissue and continues to the septal leaflet of the tricuspid valve and aortic annulus. The dotted line indicates the patch of the suture line. **D,** The double-velour Dacron (CR Bard Laboratories, Box M, Billerica, MA 01821) patch is shown in position, with the suture line completed on the crista supraventricularis. (From Laks[43]; reproduced by permission from Appleton-Century-Crofts.)

tricular septal defect is then closed (Figure 7), care being taken not to damage the conduction tissue in the posteroinferior corner of the defect. The incision in the outflow tract is then closed (Figure 8). We usually use pericardium reinforced with a Dacron mesh for the outflow tract patch. If pericardium is not available, a preclotted woven Dacron graft is used for this purpose.

After removing the patient from cardiopulmonary bypass, the right ventricular and pulmonary artery pressures are measured. If the ratio of right ventricular-to-left ventricular systolic pressure is greater than 0.65 and the pulmonary artery pressure less than 25 mm of mercury, bypass is reinstituted and the obstruction relieved by a transannular patch. Oxygen saturations are also determined to exclude a residual intracardiac shunt.

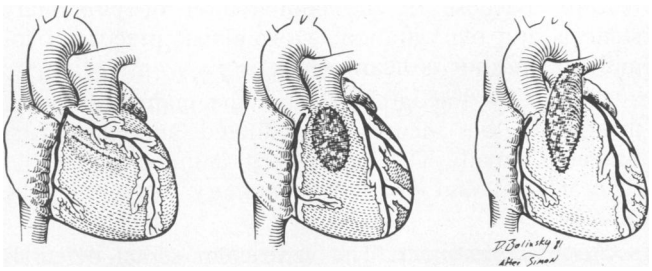

Figure 8.—Closure of the incisions. **Left,** The oblique or transverse incision is closed primarily with a double suture line. **Middle,** The vertical incision is closed with a subannular patch to enlarge the infundibular outflow tract. **Right,** The transannular incision is closed with a patch extending up to the bifurcation of the pulmonary arteries. (From Laks[43]; reproduced by permission from Appleton-Century-Crofts.)

Results of Corrective Operation

Mortality. Mortality accompanying repair of tetralogy of Fallot has decreased considerably during the past ten years. In patients younger than 1 year of age, mortality has been reported as high as 14%[25] and is higher in infants younger than 3 months of age.[15,28,32] One series of patients younger than 2 years of age had a mortality of 5%[29]; in another series the mortality among patients older than 1 year of age was 1.6%.[27]

Morbidity. Permanent heart block is now uncommon and occurs in less than 1% of surgically treated cases of tetralogy of Fallot. The presence of right bundle branch block and left anterior hemiblock may presage complete heart block.[45] Ventricular irritability may occur and cause late sudden death, as discussed later.

Residual lesions. These are discussed below, as are the long-term results of surgical correction.

Complex Tetralogy of Fallot

Under this broad term are included patients with virtual pulmonary atresia, absent pulmonary valve,[46] an atrioventricular canal defect combined with a tetralogy,[47] multiple intramuscular ventricular septal defects, a single pulmonary artery, well-developed systemic

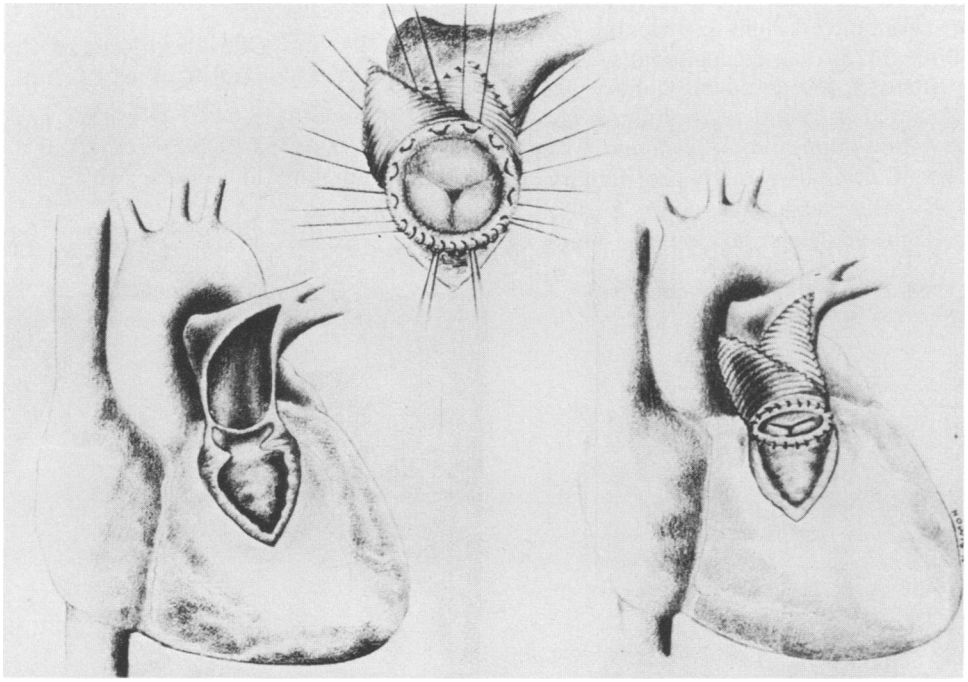

Figure 9.—Operative technique for pulmonary valve insertion beneath an outflow-tract patch. On the left, the incision extends to the bifurcation of the pulmonary artery. The inset shows the continuous sutures posteriorly and the interrupted suture line anteriorly through the patch. On the right, the valve is seen sutured beneath the patch before the completion of the patch suture line to the edges of the right ventricular incision. (From Laks[43]; reproduced by permission from Appleton-Century-Crofts.)

arterial collaterals, an aorticopulmonary window,[48] bifurcation or distal pulmonary stenosis, Epstein's anomaly and pulmonary stenosis due to previous Potts or Waterston shunts.

Tetralogy of Fallot with a single pulmonary artery. It is usually the left pulmonary artery that is absent, the left lung being supplied by systemic arterial collaterals. Whether or not a valved conduit rather than a transannular patch should be used to relieve the outflow obstruction has been considered.[49,50] A patch without a valve may be well tolerated in the absence of pulmonary hypertension or distal stenosis and if the pulmonary artery is of good size. If these conditions do not pertain, a bioprosthetic valve (either a glutaraldehyde-preserved porcine or a bovine pericardial valve) should be inserted. A valved conduit may also be used,[48] or a valve can be placed beneath an outflow-tract patch (Figure 9).[41]

Tetralogy of Fallot combined with atrioventricular canal. Pacifico and colleagues[47] studied this combined lesion in ten patients and reported good surgical results. The complete atrioventricular canal is treated in the usual fashion. Particular attention should be paid to obtaining competent mitral and tricuspid valves because tricuspid regurgitation is not tolerated well in the presence of pulmonary regurgitation or obstruction. The outflow-tract obstruction is relieved by the usual techniques. If a transannular patch is needed, a pulmonary valve should be inserted beneath the patch.

Pulmonary valve insertion. Although the severe pulmonary regurgitation accompanying a transannular patch is usually tolerated well, there is a group of patients in whom pronounced right ventricular failure develops.[51,52] Within this group are patients who have distal pulmonary stenosis, increased pulmonary vascular resistance, associated tricuspid regurgitation, absent pulmonary valve, virtual pulmonary atresia and a single pulmonary artery. Additionally, there are patients in whom some years after tetralogy repair a dilated, poorly contractile right ventricle develops. In many of these patients valved conduits have been used. We prefer placing a porcine valve in the right ventricular outflow tract beneath a patch, which avoids compression of a conduit by the sternum, and permits insertion of a larger sized valve.[53]

Absent pulmonary valve syndrome. The anatomy of absent pulmonary valve syndrome consists of a ventricular septal defect, a small pulmonary valve annulus with no valve cusps and aneurysmal dilatation of the central pulmonary arteries with small peripheral pulmonary arteries (Figure 10).

About 25% of these patients present in infancy with respiratory problems due to bronchial compression by the dilated pulmonary arteries. In others, the shunt is predominantly left to right and cyanosis is not a major feature. Because of the combination of pulmonary stenosis and regurgitation, a prominent precordial to-and-fro murmur is heard.

Studies by angiography show the main pulmonary arteries to be aneurysmally dilated and the distal branches small. The pulmonary annulus is smaller than normal and the left pulmonary artery may be missing.[54]

Surgical treatment. The ventricular septal defect is closed in the usual fashion. A valve should be inserted in the outflow tract because severe pulmonary regurgitation combined with aneurysmally dilated pulmonary arteries results in a low output state postoperatively. The valve may be placed beneath an outflow-tract patch (Figure 9). In infants who have bronchial compression, the aneurysmally dilated pulmonary arteries can be surgically narrowed.[55]

Benefits and Complications of Shunt Operations; Residua and Sequelae of Intracardiac Repair

JOHN S. CHILD, MD:* Residua and sequelae after a cardiac operation have resulted in a new and growing patient population—those with postoperative congeni-

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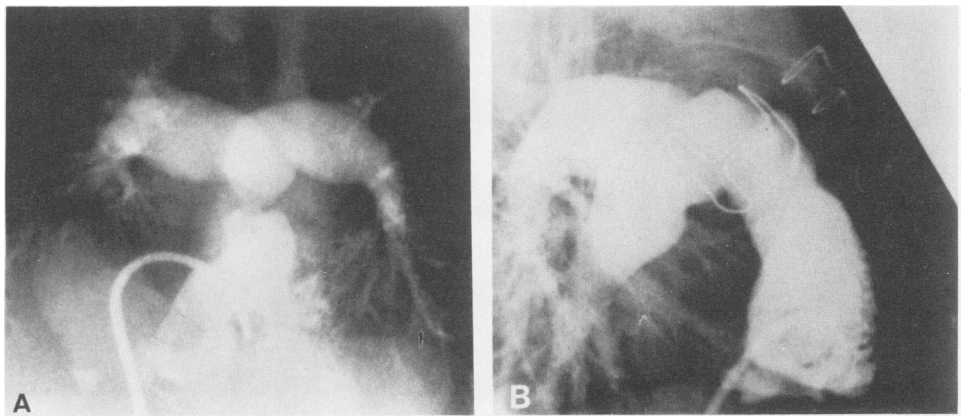

Figure 10.—Absent pulmonary valve. **A,** An anteroposterior right ventriculogram of an 8-month-old child, showing the narrowed annulus and the aneurysmally dilated main right and left pulmonary arteries with small peripheral arteries. **B,** A postoperative lateral angiogram, showing the repair with insertion of a 21-mm porcine valve beneath an outflow-tract patch. (From Laks[43]; reproduced by permission from Appleton-Century-Crofts.)

tal heart disease.[56] Patients born with tetralogy of Fallot 15 years ago had an 85% probability of being alive today and a 75% probability of living to the fourth decade.[57] Patients born today with the same condition have an even better prognosis. However, operation leaves behind obligatory abnormalities, some trivial, others serious. Proper care of adults with postoperative congenital heart disease requires knowledge of the presence, type and extent of these postoperative residua and sequelae.

Palliative Shunts

A systemic-pulmonary arterial shunt created surgically[17,18,20,58] was the first successful palliative treatment for tetralogy of Fallot. Benefits result from increased pulmonary arterial blood flow with enhanced systemic oxygen saturation; symptomatic improvement often is dramatic. Growth of underdeveloped pulmonary arteries can occur, facilitating subsequent intracardiac repair. Detrimental effects include excessive pulmonary blood flow, congestive heart failure and pulmonary vascular disease.[36,59-66] Acquired pulmonic atresia is an occasional late complication.[67] Pulmonary vascular disease is rare after Blalock-Taussig anastomoses (subclavian-pulmonary artery shunt),[59] at least for seven years.[66] The direct aortopulmonary arterial shunts (Potts, Waterston-Cooley[18,20,58]) show a higher incidence of pulmonary vascular disease, particularly the Potts procedure. Clinical findings of an excessively large anastomosis (thus warranting concern that pulmonary vascular disease may develop) include minimal or absent cyanosis; a short, low-pitched, coarse continuous murmur; progressive cardiac enlargement; increasing prominence of the pulmonary trunk and pulmonary arterial vascularity, and the appearance and progression of electrocardiographic evidence of left ventricular hypertrophy.[64] In patients with these findings, subsequent shortening or disappearance of the continuous murmur is a sign of pulmonary vascular disease.[57]

Blalock-Taussig Shunt

After a Blalock-Taussig shunt, in 4% to 6% of patients, brain abscesses develop and 2% to 5% have cerebrovascular accidents.[68,69] A subclavian steal means that collateral flow to the arm (on the side of the anastomosis) via the ipsilateral vertebral artery shunts ("steals") blood from the brain.[70] Growth of the arm on that side may be impaired, though patients are rarely aware of this. Endocarditis has been reported in as many as a third of patients before intracardiac repair.[57,71] Finally, because the size of the Blalock-Taussig anastomosis does not always grow with the patient, the effect of palliation decreases.[72]

Potts Anastomosis

Pulmonary overcirculation due to the Potts anastomosis (descending aortopulmonary arterial shunt) usually occurs in children, less often in adults.[57] On the other hand, pulmonary vascular disease is seen more frequently in adults; this sequela of operation correlates directly with the size and duration of the anastomosis.[36] Such patients are also at risk for infective endocarditis and cerebrovascular accidents.[57,70] The surgical mortality of intracardiac repair after Potts anastomosis is greater than with other types of shunts and higher than for primary intracardiac repair.[57] In addition, closure of the Potts anastomosis is technically difficult, prolonging the intracardiac repair and increasing the risk.

Waterston-Cooley Anastomosis

The Waterston-Cooley procedure (anastomosis of ascending aorta to right pulmonary artery) risks fewer sequelae than the Potts. The most frequent major complication is kinking and distortion of the right pulmonary artery, relief of which may require special reconstruction at the time of intracardiac repair.[70] Furthermore, when blood flow is restricted to one lung, the opposite lung is at increased risk of pulmonary vascular disease due to excessive blood flow.[73,74]

Intracardiac Repair

Direct intracardiac repair of tetralogy of Fallot, available for more than two decades, has evolved rapidly.[75,76] With the surgical technique now relatively standardized, attention has focused on late clinical and hemodynamic residua and sequelae and operative factors governing late morbidity and mortality.[77] Among these factors are the timing of operation, indications for a transannular patch, identification of patients at risk for late postoperative sudden death and the long-term right ventricular response to postoperative pulmonary valve incompetence.[78]

Let us now consider the sequelae of right ventriculotomy: of intraventricular closure of the ventricular septal defect; reconstruction of the right ventricular outflow tract; prosthetic materials, and residua that include right ventricular outflow obstruction, myocardial hypertrophy and right ventricular function. Complications will not be discussed.

Postoperative Sequelae

Right ventriculotomy. Incision of the right ventricular outflow tract sometimes results in ventricular aneurysm, which rarely is obvious and dramatic.[56] Of more concern is the effect of ventriculotomy on the long-term performance and functional reserve of the incised ventricle.[56,70]

During ventriculotomy injury to an anomalous coronary artery must be avoided.[79] The anterior descending or conal arteries have occasionally been injured or transected.[80]

Endocardial fibroelastosis, not only in chambers handled by the surgeon, but also in other chambers, is believed to be due to interrupted lymph drainage.[80] This sequela is not necessarily innocuous and may be responsible for late myocardial dysfunction.[80]

Conduction disturbances. Right bundle branch block, common after repair of tetralogy of Fallot.[81,82] is probably functionally benign.[70] The right bundle branch block may be due to interruption of distal or

terminal arborization of the right bundle (ventriculotomy per se) or of the proximal right bundle (repair of the ventricular septal defect).[56,83] A surface electrocardiogram is inadequate for determining the location of right bundle branch block, but intraoperative endocardial and epicardial mapping can establish the site.[84]

Bifascicular block (right bundle branch block with left anterior fascicular block) sometimes accompanies an operation (reported incidence 7% to 25%).[85-89] Most cases occur at the time of operation and persist. In some patients, the left anterior fascicular block is transient[90] but in others appears late postoperatively.[83] The prognosis of bifascicular block in this setting is controversial,[81-83] though the current consensus[77,87,88,90-93] is that sudden death due to subsequent high-degree heart block is uncommon, if not rare. Late complete heart block now occurs in 1% to 2% of patients who had intracardiac repair of Fallot's tetralogy.[85,94] The heart block can be temporary (hours to weeks in duration) or permanent and may be immediate or late (up to 14 years) postoperatively.[95-97]

The diagnosis of trifascicular conduction defects cannot be made with assurance by standard surface electrocardiography.[98] A prolonged His bundle-to-ventricle interval in the presence of right bundle branch block (with or without left anterior fascicular block) indicates infra-Hisian and usually trifascicular block, and sets the stage for subsequent complete heart block and slow ventricular escape rhythms.[99]

Ventricular arrhythmias. Until recently, sudden death after intracardiac repair of tetralogy of Fallot was ascribed to high-degree heart block (see above). This may occasionally be the case, but of equal or greater importance is electrical instability of the incised right ventricle.[77,93,100-102] Premature ventricular contractions are ominous after intracardiac repair.[57,93] Garson and associates[93] noted that 38% of their patients with premature ventricular contractions died suddenly. With exercise, especially in the postexercise recovery period, the incidence of premature beats increases (23%) and may culminate in ventricular tachycardia.[103] The most important correlation with premature ventricular contractions is elevated right ventricular systolic or end-diastolic pressure, or both.[93] The origin of inducible recurrent sustained ventricular tachycardia has been located in the right ventricular outflow tract.[83] The ventriculotomy scar coupled with increased myocardial oxygen demands of a right ventricle laboring under inadequate relief of afterload may provoke premature beats that deteriorate into sustained repetitive firing (ventricular tachycardia or fibrillation).[93] Exercise testing and ambulatory taped electrocardiography are desirable after intracardiac repair. Frequent premature beats or repetitive beats require antiarrhythmic therapy and consideration of cardiac catheterization. Reoperation for relief of significant right ventricular pressure overload might diminish the frequency and risk of premature ventricular contractions.[57] At reoperation, intraoperative endocardial mapping and resection of the reentrant pathways in offending ventricular scar should further reduce the likelihood of spontaneous ventricular tachycardia.[83]

Pulmonary regurgitation. Repair of obstruction to right ventricular outflow may leave behind pulmonary valve regurgitation (Figure 11).[56] The murmur of low pressure pulmonary regurgitation[104] is audible in up to 75% of patients after repair.[70] Long-term effects of this volume overload are uncertain.[105] Neither is it clear how well an initially thick-walled, relatively less compliant right ventricle responds if relief of obstruc-

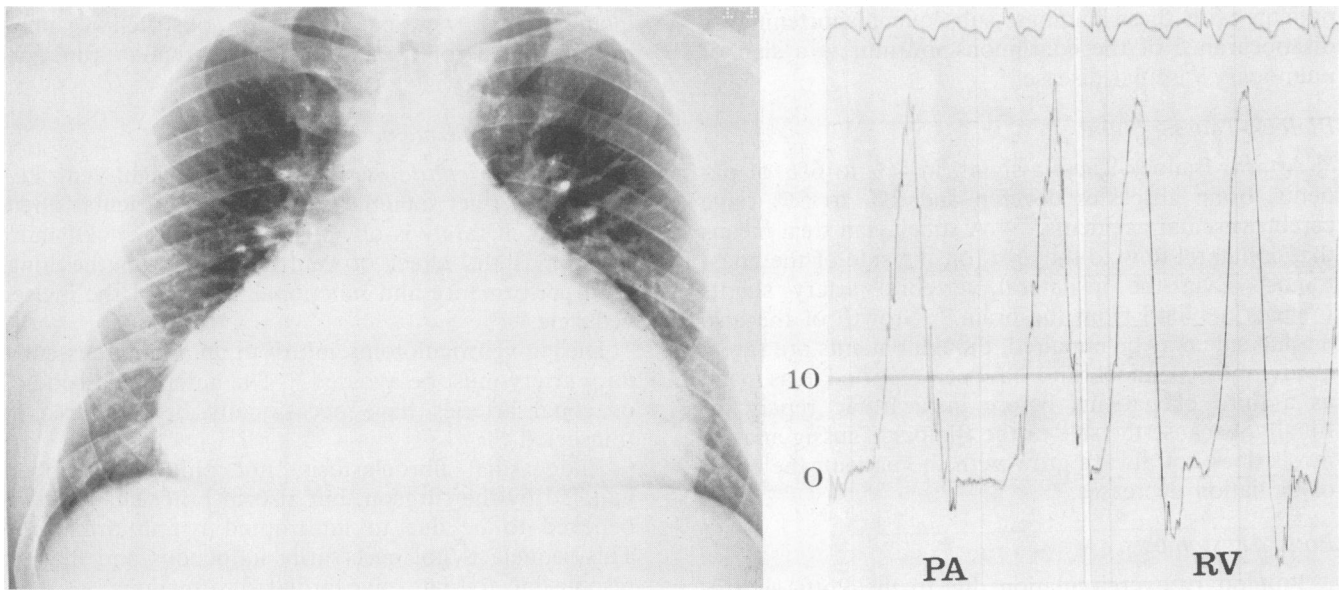

Figure 11.—Chest roentgenogram **(A)** and right heart pressure pulses **(B)** in a 30-year-old man who at 10 years of age underwent primary intracardiac repair for tetralogy of Fallot. Twenty years after operation severe pulmonary regurgitation culminated in right ventricular failure, tricuspid regurgitation and atrial flutter. The chest x-ray study shows massive cardiomegaly due to right atrial and right ventricular dilatation. The pulmonary arterial (PA) and right ventricular (RV) pressure pulses show no obstruction, identical diastolic pressures (free pulmonary regurgitation) and an early diastolic dip in the RV.

tion suddenly converts severe afterload (pressure) into moderate to pronounced preload (pulmonary regurgitation). The response of the ventricle is further complicated if repair requires not merely ventriculotomy but also an outflow or transannular patch. Thus, postoperative results depend in large part on the amount of reconstruction to which the right ventricular outflow tract is subjected[106] and the degree of residual obstruction and obligatory pulmonary regurgitation. Hemodynamic[106,107] and clinical data[70,77] indicate that most patients tolerate pulmonary incompetence well and that their exercise tolerance remains adequate *provided* there is no significant residual outflow-tract obstruction. Nonetheless, in patients who have isolated pulmonary regurgitation, late postoperative right ventricular failure sometimes develops (Figure 11).[108,109] Severe pulmonary regurgitation is associated with an elevated right ventricular end-diastolic pressure[109] exaggerated by exercise[70] or aggravated by branch stenoses of the large pulmonary arteries.[110-112] Associated tricuspid incompetence due to right ventricular failure is a serious sequela.[82,105,113]

Prosthetic Materials

Prosthetic materials used in repair include patches, artificial valves and extracardiac conduits. Follow-up studies for more than 20 years of patients in whom synthetic patches were used for closure of the ventricular septal defect, and in whom synthetic onlay or transannular patches were used for repair of the right ventricular outflow tract, have shown no significant cause for concern about durability.[77,114] However, insertion of pericardium as patch material for a ventricular septal defect has resulted in aneurysmal dilatation of the patch.[115] The early use of the Ivalon sponge was sometimes followed by reestablishment of the septal defect; occasionally aneurysms developed when this material was used as a patch for the right ventricular outflow tract.[114]

Durability, thrombogenicity, hemodynamic adequacy and a continuing threat of infective endocarditis remain concerns in the selection and implantation of prosthetic valves. Fortunately, few patients need insertion of a prosthetic pulmonary valve even when their native valve is nonfunctional after repair.[77]

Use of extracardiac conduits has made feasible the surgical correction of tetralogy of Fallot with pulmonary atresia[116]; an optimal conduit, however, is not yet available. Calcification of aortic homografts,[117] degeneration of synthetic or heterograft valves within a conduit and progressive proliferative fibrotic peel of a lumen limit the long-term outlook with current materials.[118,119]

Postoperative Residua

Right ventricular outflow gradient. Causes of residual postoperative outflow gradients include inadequate relief of subvalvular obstruction, stenosis of the valve or main pulmonary artery (at the site of a patch insertion) or stenosis of pulmonary arterial branches.[57] Ruzyllo and co-workers[106] found that only 43% of 221 catheterized postoperative patients had a right ventricular-pulmonary artery pressure gradient of less than 20 mm of mercury; however, most patients with less satisfactory relief of obstruction had few or no symptoms. Persistent stenosis postoperatively relates chiefly to the structure of the preoperative obstruction.[72] If only infundibulectomy is needed, 65% of patients have less than 20 mm of mercury gradients, but if more complex reconstruction is required, only 35% attain near complete relief of stenosis. When the postoperative right ventricular-to-left ventricular pressure ratio is more than 0.65[77] or right ventricular systolic pressure is more than 60 mm of mercury[57,106,107] (particularly in those without patch reconstruction), risk of right ventricular hypertension increases and reoperation is needed to reduce the risk of sudden death. Outflow gradients may develop or increase significantly during exercise.[120] The risk of infective endocarditis remains.

Reoperation for residua. Although in most patients the symptomatic result from intracardiac repair is satisfactory, the aforementioned points underscore that important residual lesions may remain. Symptomatic as well as asymptomatic patients with significant residual abnormalities should be recatheterized, even though firm criteria for reoperation are difficult to establish.[121-123] The most common residuum needing reoperation is the right ventricular outflow gradient. Less commonly, valve replacement for pulmonary regurgitation or reconstruction for tricuspid insufficiency is necessary.[77,105,121,122] Reoperation is occasionally needed to excise a right ventricular outflow aneurysm. Fortunately, reoperation is associated with a relatively low risk, probably no greater than that for the initial repair.[77,105,121,122,124]

Myocardial hypertrophy and ischemia. When the fetal right ventricle continues to function as a systemic pump after birth, as in cyanotic tetralogy of Fallot, right ventricular wall growth keeps pace with left ventricle and septum, and long-term function of the right ventricle is good.[125] Nevertheless, an operation done early in the natural history has important long-term objectives: normalization of ventricular mass, preservation or restoration of normal function per unit mass and to assure normal life expectancy. After intracardiac repair of Fallot's tetralogy, however, right ventricular ejection fraction during exercise may be depressed,[126-128] and abnormalities of resting right ventricular volume and ejection fraction occur in patients with large outflow patches.[127]

A continually "underloaded" left ventricle in cyanotic tetralogy of Fallot increases its volume and mass after intracardiac repair. Mild to moderate impairment of left ventricular function persists in patients not corrected in early childhood, especially those with severe prolonged cyanosis.[93,127,129] Long-term exposure of the myocardium to polycythemia and hypoxia results in myocardial ischemia. Fortunately, recent data[113,128,130,131] on adolescents and adults show normal

resting and exercise left ventricular function in most cases.

Functional responses to exercise. The average exercise capacity of postoperative patients with tetralogy of Fallot is less than normal, but individual scores vary widely even for patients with seemingly similar surgical results.[103,120,132] In these cases, exercise performance is modified by varying degrees of impaired chronotropy and reduced stroke volume.[132] As expected, patients with excellent results (normal right ventricular pressure, no outflow patch and no residual shunt) show the best functional results. Furthermore, patients who undergo intracardiac repair early in life seem to have less depression of cardiac performance with exercise[103,132] or afterload stress.[133]

Conclusion

DR PERLOFF: And now a look toward the future. Surgical improvements continue—perhaps not in quantum leaps—though most of the major dramatic breakthroughs may well have been achieved. Nevertheless, there will be a constant search for improved prosthetic materials, especially cardiac valves and conduits,[114] refinement of techniques currently used, development of new techniques and continued attention to intraoperative myocardial preservation (cardioplegia, reperfusion and so forth). In this discussion, I shall focus on some important concerns in addition to, though not necessarily apart from, the surgical improvements alluded to above; I will not confine myself to the tetralogy of Fallot and its variations. I shall briefly comment on defects uncorrected after primary repair, sequelae of ventriculotomy, electrophysiologic sequelae and residua in addition to those imposed by the ventriculotomy incision itself, valvular anatomic residua and sequelae, elevated pulmonary vascular resistance, the development and regression of increased ventricular mass and the genetics of women who survive to childbearing age after operation for congenital heart disease.[56]

Certain primary anatomic repairs leave behind uncorrected defects (residua) that may not assume physiologic importance for many decades.[56] I speak of a functionally normal bicuspid aortic valve after repair of coarctation of the aorta, mitral valve prolapse persisting after closure of an ostium secundum atrial septal defect and a cleft but competent mitral valve with a repaired ostium primum atrial septal defect.[56] In addition to the important long-term natural history of a functionally normal bicuspid aortic valve after coarctation repair, several other late postoperative concerns possibly beset these patients, namely, regulation of systemic arterial pressure, premature coronary artery disease, postoperative central nervous system complications and abnormalities of the mitral apparatus.[56] In ostium secundum atrial septal defect, the natural history of mitral valve prolapse is unclear and awaits more secure identification of *pathologic* mitral prolapse (a true developmental connective tissue fault of leaflets, annulus and chordae tendineae).[134] Regarding the cleft but competent mitral valve after primary anatomic repair of partial endocardial cushion defect, it is not yet known how susceptible that valve is to infective endocarditis or how well the leaflets, with their abnormal chordal arrangements, will retain competence during changes in left ventricular geometry in adult life.[56]

Incision of the right ventricle is used for intracardiac correction of the host of congenital lesions, one of which is the tetralogy of Fallot (see Dr Laks's remarks above). Two possible postoperative sequelae of ventriculotomy concern us, namely, the effects on ventricular electrical activity[83,85,102] and the effect on long-term myocardial contractility of the incised ventricle.[56] In addition to improving our knowledge of factors that result in electrical instability of an incised ventricle, certain important electrophysiologic sequelae follow intracardiac repair, both intra-atrial and intraventricular.[56,83] Complex intra-atrial corrections, such as Mustard's or Senning's baffle for complete transposition of the great arteries, may be followed years later by sinus node dysfunction, abnormalities of atrioventricular-node conduction, atrial flutter or atrial fibrillation.[56] Right ventriculotomy per se is responsible for two electrophysiologic concerns—electrical instability of the incised ventricle and alteration in the sequence of right ventricular activation (peripheral).[83] Intracardiac repair sometimes results in interruption of the left anterior fascicle and proximal right bundle branch (bifascicular block). Prolonged His-Purkinje conduction time (trifascicular disease) has been identified after intracardiac correction of tetralogy of Fallot.[56,83,84]

Valvular anatomic residua are necessarily present after direct repair of simple discrete valvular aortic stenosis and simple valvular pulmonic stenosis. Such valves are not morphologically normal even though the gradients may be abolished. Also, an abnormal aortic valve (with aortic regurgitation) is often left behind after uncomplicated repair of discrete subvalvular aortic stenosis.[56]

Pulmonary hypertension or, more precisely, increased pulmonary vascular resistance in operative risk and late postoperative results, continues to be a problem.[135] In certain disorders there is a special proclivity for progressive pulmonary vascular obstruction to develop, for example, endocardial cushion defects with Down's syndrome and complete transposition of the great arteries.[135] Our present knowledge of the pulmonary vascular bed has now been extended considerably beyond the pulmonary vascular disease described earlier.[135] I speak of the new approaches to morphologic analysis of this vascular bed in patients with congenital heart defects, that is, the abnormalities of arterial remodeling and growth that have been detected and quantified in early infancy.[136]

An increase in ventricular mass is perhaps the most important structural adaptation of heart muscle to overload.[125] In addition, hypoxia results in cell replication in an immature heart.[125] Both the development and regression of increased ventricular mass are being

studied. A number of points are under scrutiny, namely, normal ventricular growth (in embryo, fetus, neonate and child); the response to workloads (hemodynamic stress) and hypoxia; the cell responses of hyperplasia (increase in cell number), hypertrophy (increase in cell size) and the type of cell (muscle or connective tissue); the age or maturity of the myocardium when hemodynamic or hypoxic stress is imposed, and the biochemistry, ultrastructure and functional morphology (modeling) of the ventricles in response to volume or pressure overload.[125] The desirable physiologic adaptations to workloads must be characterized further and the transition from physiologic to pathologic states established. Regression of increased ventricular mass is being studied at the cell level (hypertrophy versus hyperplasia; muscle cells versus connective tissue cells) and at the organ level.[125] The requirements for maintaining or establishing normal ventricular function after removal of overload must be defined, together with variables such as the type and duration of preoperative hemodynamic stress, the right versus the left ventricle and the relative rates of contractile protein synthesis and degradation.[125]

There has long been concern that the growing number of postoperative congenital cardiac patients reaching childbearing age will produce a higher incidence of offspring who have congenital anomalies of the heart or circulation.[56] Accordingly, genetic investigations are being carried out.[137] Results at present show that women with congenital heart disease are at increased risk of giving birth to children with congenital cardiac anomalies, a risk not significantly affected by surgical repair and one that is considered to be of genetic importance.[137]

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